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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
|---|---|
| KRISHNAN, GANAPATHY | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1623 | |

DATE MAILED: 12/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/644,109 | STUTZMANN ET AL. | |
| | Examiner | Art Unit | |
| | Ganapathy Krishnan | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09881267.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Claim Objections*

Claim 8 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 8 recites how the low molecular weight heparin is obtained. The recitation is not further limiting. It does not matter how the heparin is obtained.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating motoneuron diseases, does not reasonably provide enablement for prevention of motoneuron diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

(A) The breadth of the claims
(B) The state of the prior art
(C) The level of one of ordinary skill
(D) The level of predictability in the art
(E) The amount of direction provided by the inventor
(F) The existence of working examples
(G) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

**The breadth of the claims**

Claims 2-19 are drawn to a method for preventing a motoneuron disease in a patient comprising administering an effective amount of low molecular weight heparin, with specific molecular weights. The scope of the claim is seen to include the administration of the said compound to a healthy patient, and subsequent exposure to conditions that would cause the motoneuron disease, wherein the said compound prevents the said exposure from manifesting itself in said patient so exposed.

**The state of the prior art**

The examiner notes that the art cited by the applicants mentions methods for preparing heparins and use of the same in treating thrombosis. Snow et al (WO 91/06303) drawn to glycosaminoglycans and proteoglycans, disclose the use of these compounds for the regeneration/treatment of neurons damaged by disorders like amyotrophic lateral sclerosis. However, there is no disclosure of potential motoneuron disease preventive activity of the compound seen in the prior art. The prior art appears to be silent with regard to preventive procedures recognized by skilled artisans in the field.

**The level of one of ordinary skill**

The skilled artisan in this field is that of an MD for chemotherapeutic administration and/or a Ph.D. skilled in the development of chemotherapeutics.

**The level of predictability in the art**

The examiner acknowledges the probability and predictability that administration of the said compounds would have a reasonable expectation of success for preventing the said disease. There is not seen sufficient data to substantiate the assertion that the said disease may be prevented by the use of the compound as instantly claimed.

**The amount of direction provided by the inventor**

The instant specification is not seen to provide enough guidance that would allow a skilled artisan to extrapolate from the disclosure and the examples provided to enable the use of the active agents to prevent motoneuron disease. The specification also fails to direct the skilled artisan in correlative prior art procedures which might provide the basis for an advance in treating motoneuron disease which induces prevention of the said disease.

**The existence of working examples**

The working examples set forth in the instant specification are drawn to data involving cells in vitro. The skilled artisan in this field would not extrapolate the preventive efficacy of the compound claimed or the use of the same in preventive methods from just this example provided. The disclosure does not show the prevention of motoneuron disease. However, it is seen to show the effect of the active agents.

**The quantity of experimentation needed to make or use the invention based on the content of the disclosure**

Indeed, in view of the information set forth, the instant disclosure is not seen to be sufficient to enable the prevention of motoneuron disease with the compound set forth in the claims. A skilled artisan would not extrapolate the preventive efficacy from the results disclosed in the examples, set forth in the instant specifications.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the term "exposing". It is not clear what this means. If it means bringing the motoneurons in contact with the heparin then the claim should be reworded to indicate this. Clarification is needed.

Claims 18 and 20 recite alphanumeric notations for the heparins. It is not clear what these notations mean. Perusal of the specification failed to clarify this either. The notations should be replaced with a chemical name or structure.

Claims, which depend from rejected base claims that are unclear or indefinite, are also rendered unclear or indefinite.

***Joint Inventors***

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Snow et al (WO 91/06303).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3-19 are drawn to methods for increasing the survival or growth of motoneurons including lateral sclerosis, amyotrophic lateral sclerosis, progressive spinal

muscular atrophy, infantile muscular atrophy using low molecular weight heparin, such as enoxaparin.

Snow et al teach pharmaceutical compositions comprising effective amounts of heparin (HN)(page 11, lines 5-9) and also disclose that the compositions of their invention can be used where nerve regeneration is desired for example patients with nerve damage. The compositions can be administered to patients in whom nerve cells have been damaged by disorders like amyotrophic lateral sclerosis (page32, line 29 through page 33, line 10). However, Snow et al do not specifically disclose the use of any individual low molecular weight heparin like enoxaparin.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use low molecular weight heparins to promote growth of motoneurons. Low molecular weight heparins comprise disaccharides that mimic heparin and are used as mimetics for treatment of thrombosis (Merck Index, 1996, 12$^{th}$, edition, #3626 and #6434). A skilled artisan would be motivated to use a art tested low molecular weight mimetic of heparin in a method for promoting nerve growth and survival as instantly claimed.

## *Conclusion*

1. Claims 1-19 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 703-305-4837. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 703-308-4624. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

GK

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600